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(FILE 'HOME' ENTERED AT 10:45:00 ON 23 JUL 2004)

FILE 'MEDLINE' ENTERED AT 10:45:40 ON 23 JUL 2004

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L1      1643314 S TUMOR OR NEOPLAS? OR TUMOUR OR CANCER
L2       218501 S INVAS? OR MIGRATION OR OUTGROWTH
L3        69051 S L1 (L) L2
L4         9068 S L3 AND INHIBIT?
L5         2094 S L4 AND ASSAY
L6          166 S L5 AND INTEGRIN
L7          166 FOCUS L6 1-
L8          166 S L7
L9           59 S L7 AND PY<=1998
L10          59 FOCUS L9 1-
L11          59 S L10
L12          33 S L10 AND (EXTRACELLULAR MATRIX)
L13          33 S L12 AND INTEGRIN
L14          33 FOCUS L13 1-
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FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED AT 10:59:42 ON 23 JUL 2004

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L15          33 S L14
L16         629 S L6
L17         251 S L16 AND PY<=1998
L18         128 S L17 AND (EXTRACELLULAR MATRIX)
L19         128 FOCUS L18 1-
L20          85 S L19 AND ALPHA?
L21          85 FOCUS L20 1-
L22          96 S L18 AND (LAMININ OR FIBRONECTIN OR AMPHOTERIN OR CADHERIN OR
L23          46 DUP REM L22 (50 DUPLICATES REMOVED)
L24          46 FOCUS L23 1-
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=> d an ti so au ab l24 3-6 8 10 13 34

L24 ANSWER 3 OF 46 MEDLINE on STN
AN 90315603 MEDLINE
TI Monoclonal antibody and synthetic peptide **inhibitors** of human **tumor** cell **migration**.
SO Cancer research, **(1990 Aug 1)** 50 (15) 4485-96.
Journal code: 2984705R. ISSN: 0008-5472.
AU Yamada K M; Kennedy D W; Yamada S S; Gralnick H; Chen W T; Akiyama S K
AB The processes of **migration** and **invasion** by human **tumor** cells are likely to involve specific cell surface receptors, such as receptors for the **extracellular matrix** molecules **fibronectin**, **laminin**, and collagen. We have examined the roles of several of these receptors using a set of monoclonal antibodies directed against the beta 1 **integrin** family, as well as a series of synthetic peptides reported to **inhibit** various interactions of each of these proteins with the cell surface. The most general **inhibitor** of **tumor** cell **migration** was found to be the anti-beta 1 monoclonal antibody 13, which **inhibited** the **migration** of human HT-1080 fibrosarcoma cells, 5637 bladder carcinoma cells, VA13 viral transformants, and HCT 116 colon carcinoma cells when **fibronectin** was the **migration** substrate. Moreover, this antibody was particularly effective in blocking cell **migration** on **laminin**, as well as **migration** within 3-dimensional collagen gels. It also **inhibited** in vitro **invasiveness** in a reconstituted basement membrane **invasion assay** (Matrigel **assay**) at concentrations as low as 1 microgram/ml. **Integrins** of the beta 1 class thus appear to play a central role in several types of **migration** by a variety of human **tumor** cell lines. Anti-alpha 5 **fibronectin** receptor monoclonal antibody 16 also significantly **inhibited** **migration** on **fibronectin**, but not on other substrates, in 3 of the 4 cell lines. Conversely, anti-alpha 2 monoclonal antibody F17 strikingly **inhibited** **migration** in 3-dimensional collagen gels, but not on other substrates, implicating the alpha 2 beta 1

integrin system in **migration** of **tumor** cells within collagenous matrices. A series of synthetic peptides previously reported to **inhibit** interactions of normal cells with **fibronectin**, **laminin**, and collagen were also tested as **inhibitors** of **tumor** cell **migration**. Peptides containing the Arg-Gly-Asp adhesive recognition signal were partially **inhibitory**, but with occasional exceptions, most other peptides had no effects on **migration**. Our results indicate the central importance of several specific beta 1 **integrins** in human **tumor** cell **migration** and show the effectiveness of monoclonal antibody treatment in blocking this process in vitro.

L24 ANSWER 4 OF 46 MEDLINE on STN
AN 96030417 MEDLINE
TI In vitro regulation of human breast **cancer** cell adhesion and **invasion** via **integrin** receptors to the **extracellular matrix**.
SO British journal of surgery, **(1995 Sep)** 82 (9) 1192-6. Journal code: 0372553. ISSN: 0007-1323.
AU Gui G P; Puddefoot J R; Vinson G P; Wells C A; Carpenter R
AB The **extracellular matrix** consists of the interstitium and the basement membrane. Cellular interaction with **fibronectin** , **laminin** and collagen provides a possible mechanism by which **cancer** cells adhere, invade and metastasize. The **integrins** are a major family of adhesion molecules that recognize epitopes on the **extracellular matrix** as ligands. These include the alpha 2 beta 1, alpha 3 beta 1, alpha v beta 1 and alpha v beta 5 **integrins**, most of which were found to be expressed on MCF-7, T47D, MDA-MB-231, ZR75-1 and Hs578T breast **cancer** cell lines. Each cell line adhered to the matrix proteins in a dose-dependent manner and was **inhibited** by monoclonal antibodies against relevant **integrins**. Only Hs578T was significantly **invasive** through **fibronectin** but both Hs578T and MDA-MB-231 invaded through **laminin** and type IV collagen in an in vitro **assay**. The **invasive** potential of these cell lines could be **inhibited** by **integrin** antibodies added to cells before incubation, but the addition of antibodies after cells were allowed to adhere to the matrix failed to **inhibit** **invasion**. **Inhibition** of cellular adhesion to the matrix reduced the **invasive** potential of breast **cancer** cell lines. As **integrin** antibodies **inhibit** cell **invasion** in vitro, the **integrins** may be of potential value as antitumour therapeutic agents.

L24 ANSWER 5 OF 46 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
AN 96:241453 SCISEARCH
TI TENASCIN MEDIATES HUMAN GLIOMA CELL-MIGRATION AND MODULATES CELL-MIGRATION ON **FIBRONECTIN**
SO JOURNAL OF CELL SCIENCE, (**MAR 1996**) Vol. 109, Part 3, pp. 643-652. ISSN: 0021-9533.
AU DERYUGINA E I; BOURDON M A (Reprint)
AB The role of tenascin in mediating **tumor** cell **migration** was studied using two cell **migration** models. In **migration/invasion** Transwell **assays** U251.3 glioma cells rapidly migrated through the 8 mu m pore size membranes onto tenascin- and **fibronectin**-coated surfaces. In this **assay** the number of cells migrating onto tenascin was 52.2+/-9.6% greater than on **fibronectin** within 4 hours. To assess cell **migration** rates and cell morphology, U251.3 **migration** was examined in a two-dimension spheroid **outgrowth assay**. The radial distance migrated by U251.3 cells from **tumor** spheroids was found to be 53.8+/-4.9% greater on tenascin than on **fibronectin**. Cells migrating on tenascin display a very motile appearance, while cells migrating on **fibronectin** spread and maintain close intercellular contacts. Cell **migration** in the presence of **integrin** blocking antibodies demonstrated that **migration** on tenascin and **fibronectin** is mediated by distinct **integrins**, alpha(2)

beta(1) and alpha(v) beta(5)/alpha(v) beta(3), respectively. Since tenascin is coexpressed in malignant **tumor** matrices with **fibronectin**, we assessed the effects of tenascin on U251.3 cell **migration** mediated by **fibronectin**. Tenascin was found to provide a positive effect on **fibronectin**-mediated **migration** by altering cell morphology and enhancing cell motility. These effects of tenascin on **fibronectin**-mediated cell **migration** were **inhibited** by blocking beta(1) and alpha(2) beta(1) **integrins**. The results suggest that tenascin may play a significant role in promoting **tumor** cell **migration** and **invasiveness** by modulating cell responses to normal matrix components.

L24 ANSWER 6 OF 46 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
AN 94:563520 SCISEARCH
TI DEVELOPMENT OF AN IN-VITRO **EXTRACELLULAR-MATRIX ASSAY** FOR STUDIES OF BRAIN-**TUMOR** CELL **INVASION**
SO JOURNAL OF NEURO-ONCOLOGY, (**1994**) Vol. 20, No. 1, pp. 1-15. ISSN: 0167-594X.
AU AMAR A P; DEARMOND S J; SPENCER D R; COOPERSMITH P E; RAMOS D M; ROSENBLUM M L (Reprint)
AB **Invasion** of brain by **tumor** cells is an inherent feature of the malignant phenotype. **Assays** to quantitate **invasiveness** should provide a powerful tool to investigate this phenomenon. We have developed a modified in vitro **assay** to measure **tumor** cell **invasion**, attachment, and chemotaxis using a barrier of the complex basement membrane Matrigel on gelatin-coated filters, Within 5 hours, 7.8% of U251MG(p) and 2.6% of SF126 human malignant glioma cells invaded the Matrigel and filter, compared with 0.8% of normal-human leptomeningeal cells. The extent of **invasion** was directly proportional to incubation time and filter pore size and inversely proportional to the Matrigel concentration. Cells from exponentially growing U251MG(p) cultures invaded more readily (10.9%) than cells from plateau-phase cultures (2.3%); however, labeling studies with bromodeoxyuridine showed that quiescent cells and rapidly dividing cells were equally capable of invading. This suggests that the mechanisms underlying **invasion** by malignant glioma cells are distinct from those underlying proliferation and indicates the need for therapy aimed specifically at **invasive** behavior. In a practical application of this **assay** to test a potential anti-**invasive** strategy, monoclonal antibodies to the beta subunit of an **integrin** receptor mediating attachment to the **extracellular matrix inhibited invasion** by U251MG(p) cells in a dose-dependent manner. This **assay** should allow evaluation of the cellular and molecular basis of brain **tumor** progression and perhaps aid the development of rationally designed drugs that limit **tumor invasion**. It may also allow prediction of the clinical behavior of **neoplasms** in individual patients.

L24 ANSWER 8 OF 46 MEDLINE on STN
AN 1999011003 MEDLINE
TI **Inhibition** of human glioblastoma cell adhesion and invasion by 4-(4'-hydroxylphenyl)-amino-6,7-dimethoxyquinazoline (WHI-P131) and 4-(3'-bromo-4'-hydroxylphenyl)-amino-6,7-dimethoxyquinazoline (WHI-P154).
SO Clinical cancer research : an official journal of the American Association for Cancer Research, (**1998 Oct**) 4 (10) 2463-71. Journal code: 9502500. ISSN: 1078-0432.
AU Narla R K; Liu X P; Klis D; Uckun F M
AB Glioblastoma multiforme is a highly **invasive** primary brain **tumor** with a disappointingly high local recurrence rate and mortality despite intensive multimodality treatment programs. Therefore, new agents that are capable of **inhibiting** the infiltration of normal brain parenchyma by glioblastoma cells are urgently needed. Here, we show that the novel quinazoline derivatives 4-(4'-hydroxylphenyl)-amino-6,7-dimethoxyquinazoline (WHI-P131) and 4-(3'-bromo-4'hydroxylphenyl)-amino-6,7-dimethoxyquinazoline (WHI-P154) are potent **inhibitors** of glioblastoma cell adhesion and **migration**. Specifically, both compounds **inhibited** at micromolar concentrations: (a) **integrin**-mediated glioblastoma cell adhesion to the

extracellular matrix proteins **laminin**, type IV collagen, and **fibronectin**; (b) **integrin**-independent epidermal growth factor-induced adhesion of glioblastoma cells to poly-L-lysine-coated tissue culture plates; (c) fetal bovine serum-induced polymerization of actin and actin stress fiber formation as well epidermal growth factor-stimulated formation of focal adhesion plaques in serum-starved glioblastoma cells; and most importantly, (d) glioblastoma cell **migration** in in vitro **assays** of **tumor** cell **invasiveness** using **tumor** cell spheroids and/or Matrigel-coated Boyden chambers. Further preclinical development of WHI-P131 and WHI-P154 may provide the basis for the design of more effective adjuvant chemotherapy programs for glioblastoma multiforme.

L24 ANSWER 10 OF 46 MEDLINE on STN
AN 97194803 MEDLINE
TI ECM dependent and **integrin** mediated **tumor** cell **migration** of human glioma and melanoma cell lines under serum-free conditions.
SO Anticancer research, **(1996 Nov-Dec)** 16 (6B) 3679-87.
Journal code: 8102988. ISSN: 0250-7005.
AU Goldbrunner R H; Haugland H K; Klein C E; Kerkau S; Roosen K; Tonn J C
AB Collagen IV, **laminin** and **fibronectin** are constituents of the cerebral **extracellular matrix** (ECM), which is critical in glioma cell **invasion**. The aim of the present study was to evaluate the **integrin** dependent cell-matrix interactions of two **tumors** with different **invasive** properties under matrixfree conditions. Two human glioma (GaMG, U373) and melanoma (MV3, BLM) cell lines were grown in serum free medium. Immunofluorescence microscopy of collagen IV, **laminin**, and **fibronectin** was performed. The adhesion of monolayer cells and their **migration** out of multicellular spheroids was quantified for these ECM components. **Integrin** chains known to act as **laminin** receptors were blocked by specific antibodies in additional **migration assays**. All cell lines expressed all the ECM components under serum free conditions. **Tumor** cell adhesion and **migration** in both glioma and melanoma cell lines was increased by all the ECM components, **laminin** being the strongest promotor of **migration**. However, **migration** was dose dependent in gliomas, whereas melanomas revealed a dose optimum of 10 micrograms/ml **laminin**. Antibodies against alpha 3 **integrins** significantly reduced **migration** on **laminin** in all cell lines, anti-beta 1 in all cell lines except U373. Anti-alpha 2 in BLM showed a strong effect, anti-alpha 6 was a stronger **inhibitor** in glioma than in melanoma cells. **Integrins** are functionally involved in **tumor** cell locomotion on **laminin**. The blocking of **laminin** related **integrin** chains markedly reduces cell motility in a varying manner between the cell lines. Moreover, different cell lines utilize different **integrins** as the **laminin** receptor.

L24 ANSWER 13 OF 46 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
AN 97:604066 SCISEARCH
TI **Inhibition** of **integrin** mediated cell adhesion of human head and neck squamous cell carcinoma to **extracellular matrix laminin** by monoclonal antibodies
SO INTERNATIONAL JOURNAL OF ONCOLOGY, (**SEP 1997**) Vol. 11, No. 3, pp. 457-464.
Publisher: INT JOURNAL ONCOLOGY, C/O PROFESSOR D A SPANDIDOS, EDITORIAL OFFICE, 1, S MERKOURI ST, ATHENS 116 35, GREECE.
ISSN: 1019-6439.
AU vanWaes C (Reprint); Surh D M; Chen Z; Carey T E
AB We recently reported that three members of the **integrin** family of cell adhesion molecules, designated alpha 2 beta 1, alpha 3 beta 1, and alpha 6 beta 4, are expressed at increased levels within the **tumors** and cell lines of patients with SCC. These three **integrins** have been reported to serve as receptors for **laminin** isoforms, and we also previously observed that **laminins** are secreted by SCC cell lines isolated from patients. In this study, the expression and localization of the three **integrins**

and **laminin** in situ was evaluated in ten **tumor** specimens from patients with SCC by immunohistochemistry using **integrin** subunit-specific monoclonal antibodies. The ability of the antibodies to **inhibit laminin** attachment of a human squamous cell carcinoma line was determined by in vitro cell adhesion **assay**. **Laminin** and the three **integrins** were co-localized along the **invasive** border of the **tumor** parenchyma in 10/10 patient **tumor** specimens. Attachment of the UM-SCC-38 cell line to **laminin** was strongly **inhibited** by specific mAbs to alpha 2 and alpha 6 **integrin** subunits alone, or completely using a combination of alpha 2, alpha 3, and alpha 6 subunit specific mAbs. The co-localization of the three abnormally expressed **integrins** and **laminin** in patient **tumor** specimens indicates the potential for interaction of these receptors and ligand in vivo. The results of the cell adhesion **assays** using a patient SCC cell line that expresses the same repertoire of **integrins** confirms that SCC attach to **laminin** isoforms primarily through the alpha 2, alpha 3 and alpha 6 subunit-containing **integrins**. These findings provide a basis for undertaking experimental studies to obtain small molecule receptor antagonists to determine the role of these **integrins** in **tumor** formation, growth, **invasion** and metastasis in vivo.

L24 ANSWER 34 OF 46 MEDLINE on STN
AN 95229698 MEDLINE
TI **Inhibitory** effects of adhesion oligopeptides on the invasion of squamous carcinoma cells with special reference to implication of alpha v **integrins**.
SO Journal of cancer research and clinical oncology, **(1995)** 121 (3) 133-40.
Journal code: 7902060. ISSN: 0171-5216.
AU Kawahara E; Imai K; Kumagai S; Yamamoto E; Nakanishi I
AB We studied invasion-related adhesion events in vitro using three squamous carcinoma cell lines (HSC-3), poorly differentiated type; OSC-19, well-differentiated type; and KB cells, undifferentiated type). An in vitro invasion **assay** through matrigel in the transwell chamber revealed that HSC-3 cells were most invasive, OSC-19 cells moderately invasive and KB cells least invasive. **Inhibition assay** of invasion using synthetic peptides RGD, RGDV, RGDS, RGDT, IKVAV and YIGSR, showed that invasion of the three cell lines was significantly **inhibited** by RGDV. There were other peptides that **inhibited** invasion significantly including IKVAV for HSC-3, and RGDS and YIGSR for OSC-19. HSC-3 cells and OSC-19 cells adhered to **fibronectin**, **laminin**, vitronectin, and type IV collagen, and KB cells did not adhere to **laminin** but did to **fibronectin**, vitronectin and collagen type IV. Pretreatment of cells with RGDV peptide in the attachment **assay** reduced the ability of these cells to bind to vitronectin and **fibronectin** more efficiently than pretreatment with RGDS. Anti-alpha v antibodies **inhibited** adhesion of HSC-3, OSC-19 and KB cells to vitronectin, but anti-beta 1 antibodies did not **inhibit** adhesion. Immunofluorescent microscopic examinations showed that all cell lines were positive for anti-beta 5 and anti-alpha v antibodies, and only HSC-3 cells were positive for anti-beta 3 antibody. alpha 5 beta 1 was not clearly demonstrated in any of the cell lines. RGDV was the most effective **inhibitor** of squamous cell carcinoma invasion among the synthetic oligopeptides used in this experiment, and it is suggested that it affects alpha v beta 3- and/or alpha v beta 5-mediated carcinoma cell invasion.

=>

L19 ANSWER 3 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1990:588996 CAPLUS
DN 113:188996
TI Monoclonal antibody and synthetic peptide **inhibitors** of human **tumor** cell **migration**
SO Cancer Research (**1990**), 50(15), 4485-96
CODEN: CNREA8; ISSN: 0008-5472
AU Yamada, Kenneth M.; Kennedy, Dorothy W.; Yamada, Susan S.; Gralnick, Harvey; Chen, Wen Tien; Akiyama, Steven K.
AB The processes of **migration** and **invasion** by human **tumor** cells are likely to involve specific cell surface receptors, such as receptors for the **extracellular matrix** mols. fibronectin, laminin, and collagen. This study examined the roles of several of these receptors using a set of monoclonal antibodies directed against the β1 **integrin** family, as well as a series of synthetic peptides reported to **inhibit** various interactions of each of these proteins with the cell surface. The most general **inhibitor** of **tumor** cell **migration** was found to be the anti-β1 monoclonal antibody 13, which **inhibited** the **migration** of human HT-1080 fibrosarcoma cells, 5637 bladder carcinoma cells, VA13 viral transformants, and HCT 116 colon carcinoma cells when fibronectin was the **migration** substrate. Moreover, this antibody was particularly effective in blocking cell **migration** on laminin, as well as **migration** within 3-dimensional collagen gels. It also **inhibited** in vitro **invasiveness** in a reconstituted basement membrane **invasion assay** (Matrigel **assay**) at concns. as low as 1 μg/mL. **Integrins** of the β1 class thus appear to play a central role in several types of **migration** by a variety of human **tumor** cell lines. Anti-α5 fibronectin receptor monoclonal antibody 16 also significantly **inhibited migration** on fibronectin, but not on other substrates, in 3 of the 4 cell lines. Conversely, anti-α2 monoclonal antibody F17 strikingly **inhibited migration** in 3-dimensional collagen gels, but not on other substrates, implicating the α2β1 **integrin** system in **migration** of **tumor** cells within collagenous matrixes. A series of synthetic peptides previously reported to **inhibit** interactions of normal cells with fibronectin, laminin, and collagen were also tested as **inhibitors** of **tumor** cell **migration**. Peptides containing the Arg-Gly-Asp adhesive recognition signal were partially **inhibitory**, but with occasional exceptions, most other peptides had no effects on **migration**. The results indicate the central importance of several specific β1 **integrins** in human **tumor** cell **migration** and show the effectiveness of monoclonal antibody treatment in blocking this process in vitro.

L19 ANSWER 4 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:398775 CAPLUS
DN 127:93491
TI Role of **integrins** and evidence for two distinct mechanisms mediating human colorectal carcinoma cell interaction with peritoneal mesothelial cells and **extracellular matrix**
SO Cell Adhesion and Communication (**1997**), 4(6), 439-455
CODEN: CADCEF; ISSN: 1061-5385
AU Schlaeppi, Marc; Ruegg, Curzio; Tran-Thang, Chien; Chapuis, Germain; Tevaearai, Hendrik; Lahm, Harald; Sordat, Bernard
AB Peritoneal carcinomatosis involves a series of events including **tumor** cell interactions with mesothelial cells and the **extracellular matrix** (ECM). The authors have studied the adhesive and **invasive** properties of four human colorectal carcinoma cell lines (Co115, HT29, SW480, SW620) confronted in vitro with a human mesothelial cell monolayer or with the ECM proteins collagen IV, laminin-1, fibronectin, tenascin-C and vitronectin. Quantitation was achieved following staining of **tumor** cells with the calcein-AM fluorescent dye. The authors found that all four cell lines rapidly adhered to a mesothelial cell monolayer. This adhesion event was not **inhibitable** by anti-**integrin** and anti-CD44 antibodies. Following initial attachment, the SW480 and SW620 cells invaded the mesothelial cell monolayer more aggressively than HT29 and Co115 cells. All cell lines adhered to ECM proteins with each one exhibiting an individual adhesion pattern. Adhesion to matrix was completely **integrin**-dependent. When tested in an **invasion assay**, HT29 and Co115 cells crossed Matrigel-coated filters, whereas SW480 and SW620 cells did not. This **invasion** was **inhibited** by anti-β1 **integrin** antibodies. Thus, the initial colorectal **tumor** cell-mesothelial cell interaction occurs through an **integrin**-independent mechanism whereas adhesion to matrix proteins and **invasion** through Matrigel are **integrin**-dependent events. Furthermore, the different **invasive** capacity of SW480 and SW620 vs. HT29 and Co115 cells upon interaction with a mesothelial cell monolayer or Matrigel suggests that these two **invasion** events may be mediated by distinct mechanisms.

L19 ANSWER 5 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:567717 CAPLUS
DN 127:232741
TI **Inhibition** of **integrin** mediated cell adhesion of human head and neck squamous cell carcinoma (SCC) to **extracellular matrix** laminin by monoclonal antibodies
SO International Journal of Oncology (**1997**), 11(3), 457-464
CODEN: IJONES; ISSN: 1019-6439
AU Van Waes, Carter; Surh, Dong Mi; Chen, Zhong; Carey, Thomas E.
AB The authors recently reported that 3 members of the **integrin** family of cell adhesion mols., designated α2β1, α3β1, and α6β4, are expressed at increased levels within the **tumors** and cell lines of patients with SCC. These 3 **integrins** have been reported to serve as receptors for laminin isoforms, and the authors also previously observed that laminins are secreted by SCC cell lines isolated from patients. Here, the expression and localization of the 3 **integrins** and laminin in situ was evaluated in 10 **tumor** specimens from patients with SCC by immunohistochem. using **integrin** subunit-specific monoclonal antibodies. The ability of the antibodies to **inhibit** laminin attachment of a human squamous cell carcinoma line was determined by in vitro cell adhesion **assay**. Laminin and the 3 **integrins** were co-localized along the **invasive** border of the **tumor** parenchyma in 10/10 patient **tumor** specimens. Attachment of the UM-SCC-38 cell line to laminin was strongly **inhibited** by specific mAbs to α2 and α6 **integrin** subunits alone, or completely using a combination of α2, α3, and α6 subunit specific mAbs. The co-localization of the 3 abnormally expressed **integrins** and laminin in patient **tumor** specimens indicates the potential for interaction of these receptors and ligand in vivo. The results of the cell adhesion **assays** using a patient SCC cell line that expresses the same repertoire of **integrins** confirms that SCC attach to laminin isoforms primarily through the α2, α3, and α6 subunit-containing **integrins**. These findings provide a basis for undertaking exptl. studies to obtain small mol. receptor antagonists to determine the role of these **integrins** in **tumor** formation, growth, **invasion**, and metastasis in vivo.

L14 ANSWER 9 OF 33 MEDLINE on STN
AN 97034559 MEDLINE
TI A novel monoclonal antibody, L1A3, is directed to the functional site of the alpha v **integrin** subunit.
SO Hybridoma, **(1996 Aug)** 15 (4) 279-88.
Journal code: 8202424. ISSN: 0272-457X.
AU Deryugina E I; Strongin A; Yu C; Bourdon M A
AB We have generated a monoclonal antibody (MAb) L1A3 directed to the alpha v **integrin** subunit as shown by competitive binding with other anti-alpha v-specific MAbs and immunodepletion. MAb L1A3 is a function-blocking antibody **inhibiting** cell adhesion to the **extracellular matrix** proteins, fibronectin and vitronectin. Adherence to vitronectin of all cells studied including normal dermal microvascular endothelial cells and three **tumor** cell lines was **inhibited** in the presence of MAb L1A3. However, the contribution of the alpha v **integrin** subunit in mediating adhesion to fibronectin was dependent on the cell line, as indicated by differences in the **inhibition** of cell adhesion with MAb L1A3 and alpha 5 beta 1 **integrin** subunit blocking MAb P1D6. Glioma U251.3 cell adhesion to fibronectin was blocked by either MAb L1A3 or MAb P1D6 while fibrosarcoma HT1080 cells were blocked with MAb P1D6 only. **Tumor** cell **migration** mediated by vitronectin and fibronectin is blocked by MAb L1A3 in the two-dimensional spheroid **outgrowth assay**. Microvascular endothelial cell transwell membrane **migration** onto the fibronectin was also blocked by MAb L1A3. Comparison of the **integrins** involved in U251.3 cell **migration** on fibronectin or tenascin using a panel of **integrin** blocking MAbs including MAb L1A3 showed that only a subset of **integrins** participating in cell adhesion is essential for cell **migration** and these **integrins** appear to be ligand specific. Fibronectin-mediated **tumor** cell **migration** was critically dependent on alpha v **integrins** as shown by L1A3 blocking of **migration** while the beta 1 **integrins** were absolutely necessary for tenascin-mediated cell **migration**.

L14 ANSWER 7 OF 33 MEDLINE on STN
AN 97194803 MEDLINE
TI ECM dependent and **integrin** mediated **tumor** cell **migration** of human glioma and melanoma cell lines under serum-free conditions.
SO Anticancer research, **(1996 Nov-Dec)** 16 (6B) 3679-87.
Journal code: 8102988. ISSN: 0250-7005.
AU Goldbrunner R H; Haugland H K; Klein C E; Kerkau S; Roosen K; Tonn J C
AB Collagen IV, laminin and fibronectin are constituents of the cerebral **extracellular matrix** (ECM), which is critical in glioma cell **invasion**. The aim of the present study was to evaluate the **integrin** dependent cell-matrix interactions of two **tumors** with different **invasive** properties under matrixfree conditions. Two human glioma (GaMG, U373) and melanoma (MV3, BLM) cell lines were grown in serum free medium. Immunofluorescence microscopy of collagen IV, laminin, and fibronectin was performed. The adhesion of monolayer cells and their **migration** out of multicellular spheroids was quantified for these ECM components. **Integrin** chains known to act as laminin receptors were blocked by specific antibodies in additional **migration assays**. All cell lines expressed all the ECM components under serum free conditions. **Tumor** cell adhesion and **migration** in both glioma and melanoma cell lines was increased by all the ECM components, laminin being the strongest promotor of **migration**. However, **migration** was dose dependent in gliomas, whereas melanomas revealed a dose optimum of 10 micrograms/ml laminin. Antibodies against alpha 3 **integrins** significantly reduced **migration** on laminin in all cell lines, anti-beta 1 in all cell lines except U373. Anti-alpha 2 in BLM showed a strong effect, anti-alpha 6 was a stronger **inhibitor** in glioma than in melanoma cells. **Integrins** are functionally involved in **tumor** cell locomotion on laminin. The blocking of laminin related **integrin** chains markedly reduces cell motility in a varying manner between the cell lines. Moreover, different cell lines utilize different **integrins** as the laminin receptor.

L14 ANSWER 3 OF 33 MEDLINE on STN
AN 96030417 MEDLINE
TI In vitro regulation of human breast **cancer** cell adhesion and **invasion** via **integrin** receptors to the **extracellular matrix**.
SO British journal of surgery, **(1995 Sep)** 82 (9) 1192-6.
Journal code: 0372553. ISSN: 0007-1323.
AU Gui G P; Puddefoot J R; Vinson G P; Wells C A; Carpenter R
AB The **extracellular matrix** consists of the interstitium and the basement membrane. Cellular interaction with fibronectin, laminin and collagen provides a possible mechanism by which **cancer** cells adhere, invade and metastasize. The **integrins** are a major family of adhesion molecules that recognize epitopes on the **extracellular matrix** as ligands. These include the alpha 2 beta 1, alpha 3 beta 1, alpha v beta 1 and alpha v beta 5 **integrins**, most of which were found to be expressed on MCF-7, T47D, MDA-MB-231, ZR75-1 and Hs578T breast **cancer** cell lines. Each cell line adhered to the matrix proteins in a dose-dependent manner and was **inhibited** by monoclonal antibodies against relevant **integrins**. Only Hs578T was significantly **invasive** through fibronectin but both Hs578T and MDA-MB-231 invaded through laminin and type IV collagen in an in vitro **assay**. The **invasive** potential of these cell lines could be **inhibited** by **integrin** antibodies added to cells before incubation, but the addition of antibodies after cells were allowed to adhere to the matrix failed to **inhibit invasion**. **Inhibition** of cellular adhesion to the matrix reduced the **invasive** potential of breast **cancer** cell lines. As **integrin** antibodies **inhibit** cell **invasion** in vitro, the **integrins** may be of potential value as antitumour therapeutic agents.

L14 ANSWER 2 OF 33 MEDLINE on STN
AN 90315603 MEDLINE
TI Monoclonal antibody and synthetic peptide **inhibitors** of human **tumor** cell **migration**.
SO Cancer research, **(1990 Aug 1)** 50 (15) 4485-96.
Journal code: 2984705R. ISSN: 0008-5472.
AU Yamada K M; Kennedy D W; Yamada S S; Gralnick H; Chen W T; Akiyama S K
AB The processes of **migration** and **invasion** by human **tumor** cells are likely to involve specific cell surface receptors, such as receptors for the **extracellular matrix** molecules fibronectin, laminin, and collagen. We have examined the roles of several of these receptors using a set of monoclonal antibodies directed against the beta 1 **integrin** family, as well as a series of synthetic peptides reported to **inhibit** various interactions of each of these proteins with the cell surface. The most general **inhibitor** of **tumor** cell **migration** was found to be the anti-beta 1 monoclonal antibody 13, which **inhibited** the **migration** of human HT-1080 fibrosarcoma cells, 5637 bladder carcinoma cells, VA13 viral transformants, and HCT 116 colon carcinoma cells when fibronectin was the **migration** substrate. Moreover, this antibody was particularly effective in blocking cell **migration** on laminin, as well as **migration** within 3-dimensional collagen gels. It also **inhibited** in vitro **invasiveness** in a reconstituted basement membrane **invasion assay** (Matrigel **assay**) at concentrations as low as 1 microgram/ml. **Integrins** of the beta 1 class thus appear to play a central role in several types of **migration** by a variety of human **tumor** cell lines. Anti-alpha 5 fibronectin receptor monoclonal antibody 16 also significantly **inhibited** **migration** on fibronectin, but not on other substrates, in 3 of the 4 cell lines. Conversely, anti-alpha 2 monoclonal antibody F17 strikingly **inhibited migration** in 3-dimensional collagen gels, but not on other substrates, implicating the alpha 2 beta 1 **integrin** system in **migration** of **tumor** cells within collagenous matrices. A series of synthetic peptides previously reported to **inhibit** interactions of normal cells with fibronectin, laminin, and collagen were also tested as **inhibitors** of **tumor** cell **migration**. Peptides containing the Arg-Gly-Asp adhesive recognition signal were partially **inhibitory**, but with occasional exceptions, most other peptides had no effects on **migration**. Our results indicate the central importance of several specific beta 1 **integrins** in human **tumor** cell **migration** and show the effectiveness of monoclonal antibody treatment in blocking this process in vitro.

L14 ANSWER 1 OF 33 MEDLINE on STN
AN 95105899 MEDLINE
TI Development of an in vitro **extracellular matrix** **assay** for studies of brain **tumor** cell **invasion**
.
SO Journal of neuro-oncology, **(1994)** 20 (1) 1-15.
Journal code: 8309335. ISSN: 0167-594X.
AU Amar A P; DeArmond S J; Spencer D R; Coopersmith P F; Ramos D M; Rosenblum M L
AB **Invasion** of brain by **tumor** cells is an inherent feature of the malignant phenotype. **Assays** to quantitate **invasiveness** should provide a powerful tool to investigate this phenomenon. We have developed a modified in vitro **assay** to measure **tumor** cell **invasion**, attachment, and chemotaxis using a barrier of the complex basement membrane Matrigel on gelatin-coated filters. Within 5 hours, 7.8% of U251MGp and 2.6% of SF126 human malignant glioma cells invaded the Matrigel and filter, compared with 0.8% of normal human leptomeningeal cells. The extent of **invasion** was directly proportional to incubation time and filter pore size and inversely proportional to the Matrigel concentration. Cells from exponentially growing U251MGp cultures invaded more readily (10.9%) than cells from plateau-phase cultures (2.3%); however, labeling studies with bromodeoxyuridine showed that quiescent cells and rapidly dividing cells were equally capable of invading. This suggests that the mechanisms underlying **invasion** by malignant glioma cells are distinct from those underlying proliferation and indicates the need for therapy aimed specifically at **invasive** behavior. In a practical application of this **assay** to test a potential anti-**invasive** strategy, monoclonal antibodies to the beta subunit of an **integrin** receptor mediating attachment to the **extracellular** **matrix inhibited invasion** by U251MGp cells in a dose-dependent manner. This **assay** should allow evaluation of the cellular and molecular basis of brain **tumor** progression and perhaps aid the development of rationally designed drugs that limit **tumor invasion**. It may also allow prediction of the clinical behavior of **neoplasms** in individual patients.

L14 ANSWER 9 OF 33 MEDLINE on STN
AN 97034559 MEDLINE
TI A novel monoclonal antibody, L1A3, is directed to the functional site of the alpha v **integrin** subunit.
SO Hybridoma, **(1996 Aug)** 15 (4) 279-88.
Journal code: 8202424. ISSN: 0272-457X.
AU Deryugina E I; Strongin A; Yu C; Bourdon M A
AB We have generated a monoclonal antibody (MAb) L1A3 directed to the alpha v **integrin** subunit as shown by competitive binding with other anti-alpha v-specific MAbs and immunodepletion. MAb L1A3 is a function-blocking antibody **inhibiting** cell adhesion to the **extracellular matrix** proteins, fibronectin and vitronectin. Adherence to vitronectin of all cells studied including normal dermal microvascular endothelial cells and three **tumor** cell lines was **inhibited** in the presence of MAb L1A3. However, the contribution of the alpha v **integrin** subunit in mediating adhesion to fibronectin was dependent on the cell line, as indicated by differences in the **inhibition** of cell adhesion with MAb L1A3 and alpha 5 beta 1 **integrin** subunit blocking MAb P1D6. Glioma U251.3 cell adhesion to fibronectin was blocked by either MAb L1A3 or MAb P1D6 while fibrosarcoma HT1080 cells were blocked with MAb P1D6 only. **Tumor** cell **migration** mediated by vitronectin and fibronectin is blocked by MAb L1A3 in the two-dimensional spheroid **outgrowth assay**. Microvascular endothelial cell transwell membrane **migration** onto the fibronectin was also blocked by MAb L1A3. Comparison of the **integrins** involved in U251.3 cell **migration** on fibronectin or tenascin using a panel of **integrin** blocking MAbs including MAb L1A3 showed that only a subset of **integrins** participating in cell adhesion is essential for cell **migration** and these **integrins** appear to be ligand specific. Fibronectin-mediated **tumor** cell **migration** was critically dependent on alpha v **integrins** as shown by L1A3 blocking of **migration** while the beta 1 **integrins** were absolutely necessary for tenascin-mediated cell **migration**.

L Number	Hits	Search Text	DB	Time stamp
-	18	(Receptor SAME (advanced ADJ glycation)) and RAGE	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2002/05/16 10:39
-	42	RAGE and (advanced ADJ glycation)	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2003/03/27 14:15
-	34	(Receptor SAME (advanced ADJ glycation)) and (cancer or tumor or mata$10 or neoplas$5)	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2003/03/28 15:25
-	77	Receptor SAME (advanced ADJ glycation)	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2003/03/27 16:17
-	49	Receptor ADJ advanced ADJ glycation	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2003/03/27 14:47
-	5	(US-20020002203-$ or US-20010053357-$ or US-20010039256-$).did. or (WO-9918987-$).did. or (US-20010039256-$ or WO-200020458-$ or WO-200020621-$ or WO-9954485-$ or US-20010053357-$).did.	US-PGPUB; EPO; DERWENT	2003/03/27 14:45
-	4	(Receptor ADJ advanced ADJ glycation) SAME amphoterin	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2003/03/27 14:53
-	15	Morser ADJ Michael ADJ John	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2003/03/27 14:54
-	29	(US-6465422-$ or US-5864018-$ or US-5811401-$).did. or (US-20010039256-$ or US-20020002203-$ or US-20010053357-$ or US-20030059423-$ or US-20030037344-$ or US-20030032663-$ or US-20020177550-$ or US-20020122799-$ or US-20020116725-$ or US-20020106726-$ or US-20020013256-$ or US-20010041349-$).did. or (WO-9918987-$ or WO-9954485-$ or WO-9907402-$ or WO-9822138-$ or WO-9726913-$ or WO-9739121-$).did. or (WO-200020621-$ or WO-200020458-$ or WO-200274805-$ or WO-200230889-$ or US-20020116725-$ or US-20020106726-$ or US-6465422-$ or US-20010039256-$ or US-20010053357-$).did.	USPAT; US-PGPUB; EPO; DERWENT	2003/03/27 14:56
-	87	Receptor SAME advanced SAME glycation	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2003/03/27 16:18
-	0	(Receptor SAME advanced SAME glycation) and (extracelular SAME matri$5)	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2003/03/27 16:19
-	26	(Receptor SAME advanced SAME glycation) and (laminin fibronectin amphoterin caderin integrin hyaluronic integrin amphoterin)	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2003/03/27 16:26

-	104	RAGE and (laminin fibronectin amphoterin caderin integrin hyaluronic integrin amphoterin)	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2003/03/27 16:26
-	99	(advanced ADJ glycation) and (cancer or tumor or mata$10 or neoplas$5)	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2003/03/28 15:25
-	143	invasion SAME tumor SAME integrin	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/01 15:32
-	0	integrin WITH ligand WITH vironectin	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/02 13:46
-	1587	integrin WITH ligand	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/02 15:57
-	180	(integrin WITH ligand) and (tumor WITH invasion)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/02 13:47
-	5	(((integrin WITH ligand) and (tumor WITH invasion)) and assay) and RDG	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/02 13:47
-	175	((integrin WITH ligand) and (tumor WITH invasion)) and assay	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/02 14:19
-	120	(integrin WITH ligand) and (tumor WITH cell WITH invasion)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/02 14:23
-	115	((integrin WITH ligand) and (tumor WITH cell WITH invasion)) and alpha	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/02 14:52
-	10	K1735 NEAR melanoma	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/02 14:57
-	274	Invasion NEAR assay	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/02 14:57
-	71	(Invasion NEAR assay) and integrin	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/02 14:58
-	64	((Invasion NEAR assay) and integrin) and alpha$5	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/02 14:59
-	64	((Invasion NEAR assay) and integrin) and alpha	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/02 14:59
-	22	((Invasion NEAR assay) and integrin) and (alpha WITH integrin)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/02 15:31
-	0	Rouslahti NEAR Erkki.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/02 15:32

-	109	Ruoslahti NEAR Erkki.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/02 15:46
-	43	(Ruoslahti NEAR Erkki.in.) and integrin	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/02 15:50
-	15	((Ruoslahti NEAR Erkki.in.) and integrin) and invasion	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/02 15:50
-	16	(integrin WITH ligand) and RDG	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/02 16:02
-	30	Dominguez NEAR Celia.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/02 16:02
-	2	(Dominguez NEAR Celia.in.) and integrin	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/02 16:03
-	43	Schmidt NEAR ann	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/23 08:37
-	7	tumor ADJ invasion ADJ assay	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/23 08:45
-	488	cell ADJ migration ADJ assay	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/23 08:47
-	465	(cell ADJ migration ADJ assay) and (tumor cancer)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/23 08:47
-	271	((cell ADJ migration ADJ assay) and (tumor cancer)) and (extracellular ADJ matrix)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/23 08:47
-	207	(((cell ADJ migration ADJ assay) and (tumor cancer)) and (extracellular ADJ matrix)) and integrin	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/23 10:32
-	1	((((cell ADJ migration ADJ assay) and (tumor cancer)) and (extracellular ADJ matrix)) and integrin) AND tumor ADJ inhibition	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/23 10:33